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|-------|-----|------|-----|--|
|       |     |      |     |  |
| NEWS  | 1   |      |     | Web Page for STN Seminar Schedule - N. America                                     |
| NEWS  |     | APR  |     | STN AnaVist, Version 1, to be discontinued   |
| NEWS  | 3   | APR  | 15  | WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats          |
| NETTO | 4   | APR  | 00  | EMBASE Controlled Term thesaurus enhanced  |
| NEWS  |     | APR  |     | IMSRESEARCH reloaded with enhancements   |
| NEWS  |     | MAY  |     | INPAFAMDB now available on STN for patent family                                   |
| NEWS  | ь   | PLMI | 30  | searching  |
| NEWS  | 7   | MAY  | 30  | DGENE, PCTGEN, and USGENE enhanced with new homology                               |
|       |     |      |     | sequence search option   |
| NEWS  | 8   | JUN  | 06  | EPFULL enhanced with 260,000 English abstracts                                     |
| NEWS  | 9   | JUN  | 06  | KOREAPAT updated with 41,000 documents   |
| NEWS  | 10  | JUN  | 13  | USPATFULL and USPAT2 updated with 11-character                                     |
|       |     |      |     | patent numbers for U.S. applications   |
| NEWS  | 11  | JUN  | 19  | CAS REGISTRY includes selected substances from                                     |
|       |     |      |     | web-based collections  |
| NEWS  | 12  | JUN  | 25  | CA/CAplus and USPAT databases updated with IPC                                     |
|       |     |      |     | reclassification data  |
| NEWS  | 13  | JUN  | 30  | AEROSPACE enhanced with more than 1 million U.S.                                   |
|       |     |      |     | patent records   |
| NEWS  | 14  | JUN  | 30  | EMBASE, EMBAL, and LEMBASE updated with additional                                 |
|       |     |      |     | options to display authors and affiliated  |
|       |     |      |     | organizations  |
| NEWS  | 15  | JUN  | 30  | STN on the Web enhanced with new STN AnaVist                                       |
|       |     |      |     | Assistant and BLAST plug-in  |
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| NEWS  |     | JUL  |     | CA/CAplus patent coverage enhanced   |
| NEWS  | 18  | JUL  | 28  | EPFULL enhanced with additional legal status information from the epoline Register |
| NEWS  | 10  | JUL  | 20  | IFICDB, IFIPAT, and IFIUDB reloaded with enhancements                              |
| NEWS  |     | JUL  |     | STN Viewer performance improved  |
| NEWS  |     | AUG  |     | INPADOCDB and INPAFAMDB coverage enhanced  |
| NEWS  |     | AUG  |     | CA/CAplus enhanced with printed Chemical Abstracts                                 |
| MEMO  | 22  | AUG  | 13  | page images from 1967-1998   |
| NEWS  | 23  | AUG  | 15  | CAOLD to be discontinued on December 31, 2008                                      |
| NEWS  | 24  | AUG  | 15  | CAplus currency for Korean patents enhanced  |
| NEWS  | 25  | AUG  | 25  | CA/CAplus, CASREACT, and IFI and USPAT databases                                   |
|       |     |      |     | enhanced for more flexible patent number searching                                 |
| NEWS  | 26  | AUG  | 27  | CAS definition of basic patents expanded to ensure                                 |
|       |     |      |     | comprehensive access to substance and sequence                                     |
|       |     |      |     | information  |

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1 2 3 4 5 6 7 8
ring nodes :
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
chain bonds :
1-2 2-3 3-4 4-5 4-6 6-7 6-8 8-12 9-15 19-24
ring bonds :
9-10 9-14 10-11 11-12 12-13 13-14 15-16 15-19 16-17 17-18 18-19 20-21
20-25 21-22 22-23 23-24 24-25
exact/norm bonds :
1-2 2-3 3-4 4-5 4-6 6-8 9-15 15-16 15-19 16-17
exact bonds :
6-7 8-12 17-18 18-19 19-24
normalized bonds :
9-10 9-14 10-11 11-12 12-13 13-14 20-21 20-25 21-22 22-23 23-24 24-25
isolated ring systems :
containing 9 : 15 : 20 :
```

Match level:
1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:CLASS 9:Atom 10:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 20

22:Atom 23:Atom 24:Atom 25:Atom

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chain nodes :

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=> s L1 SSS full

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L2 4 SEA SSS FUL L1

1.3 3 L2

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L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:370913 CAPLUS Full-text DOCUMENT NUMBER: 140:375166

Preparation of nitric oxide releasing selective TITLE:

4 ANSWERS

cyclooxygenase-2 inhibitors

INVENTOR(S): Wang, Zhaoyin; Young, Robert N.; Zamboni, Robert

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Pat.ent. English

LANGUAGE: FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT  | NO.  | KIN                                       | D                 | DATE  |   |                   |   |   | ION :   | DATE  |                   |  |  |                                       |     |  |  |
|---|--|---|-------------------|---|---|-------------------|---|---|---|---|-------------------|--|--|---------------------------------------|-----|--|--|
| WO 2004   | 037798   | A1 200                                    |                   |   | 0506  |                   |   |   |   | 20031021  |                   |  |  |                                       |     |  |  |
| W:  | AE, AG,  | AL,                                       | AM,               | AT,   | AU,   | AZ,               | BA,   | BB,   | BG,   | BR,   | BY,               | BZ,  | CA,  | CH,                                   | CN, |  |  |
|   | CO, CR,  | CU,                                       | CZ,               | DE,   | DK,   | DM,               | DZ,   | EC,   | EE,   | EG,   | ES,               | FI,  | GB,  | GD,                                   | GE, |  |  |
|   | GH, GM,  | HR,                                       | HU,               | ID,   | IL,   | IN,               | IS,   | JP,   | KE,   | KG,   | KR,               | KZ,  | LC,  | LK,                                   | LR, |  |  |
|   | LS, LT,  | LU,                                       | LV,               | MA,   | MD,   | MG,               | MK,   | MN,   | MW,   | MX,   | MZ,               | NI,  | NO,  | NZ,                                   | OM, |  |  |
|   | PG, PH,  | PL,                                       | PT,               | RO,   | RU,   | SC,               | SD,   | SE,   | SG,   | SK,   | SL,               | SY,  | TJ,  | TM,                                   | TN, |  |  |
|   | TR, TT,  | TZ,                                       | UA,               | UG,   | US,   | UZ,               | VC,   | VN,   | YU,   | ZA,   | ZM,               | ZW   |  |                                       |     |  |  |
| RW:   | GH, GM,  | KE,                                       | LS,               | MW,   | MZ,   | SD,               | SL,   | SZ,   | TZ,   | UG,   | ZM,               | ZW,  | AM,  | AZ,                                   | BY, |  |  |
|   | KG, KZ,  | MD,                                       | RU,               | ΤJ,   | TM,   | AT,               | BE,   | BG,   | CH,   | CY,   | CZ,               | DE,  | DK,  | EE,                                   | ES, |  |  |
|   | FI, FR,  | GB,                                       | GR,               | HU,   | IE,   | IT,               | LU,   | MC,   | NL,   | PT,   | RO,               | SE,  | SI,  | SK,                                   | TR, |  |  |
|   | BF, BJ,  | CF,                                       | CG,               | CI,   | CM,   | GA,               | GN,   | GQ,   | GW,   | ML,   | MR,               | NE,  | SN,  | TD,                                   | TG  |  |  |
| CA 2503   | 063  |   | A1                |   | 2004  | 0506              |   | CA 2  | 003-  | 2503  | 20031021          |  |  |                                       |     |  |  |
| AU 2003   | 278039   |   | A1 20040513       |   |   |                   |   | AU 2  | 003-  | 2780  | 20031021          |  |  |                                       |     |  |  |
| EP 1562   | 914  |   | A1 2005081        |   |   |                   | EP 2003-769122  |   |   |   |                   |  | 20031021   |                                       |     |  |  |
| R:  | AT, BE,  | CH,                                       | DE,               | DK,   | ES,   | FR,               | GB,   | GR,   | IT,   | LI,   | LU,               | NL,  | SE,  | MC,                                   | PT, |  |  |
|   | IE, SI,  | LT,                                       | LV,               | FI,   | RO,   | MK,               | CY,   | AL,   | TR,   | BG,   | CZ,               | EE,  | HU,  | SK                                    |     |  |  |
| US 2006   | 0058363  |   | A1                |   | 2006  | 0316              | US 2005-530214  |   |   |   |                   | 20050404                                     |  |                                       |     |  |  |
| PRIORITY APP  | PRIORITY APPLN. INFO.:   |   |                   |   |   |                   |   | US 2  | 002-  | 4202  | 92P               |  | P 2  | 0021                                  | 022 |  |  |
|   |  |   |                   |   |   |                   |   | WO 2  | 003-  | CA16  | 05                |  | W 2  | 0031                                  | 021 |  |  |
| OTHER SOURCE  | OTHER SOURCE(S):   |   |                   |   |   |                   | 66  |   |   |   |                   |  |  |                                       |     |  |  |
| AU 2003<br>EP 1562<br>R:<br>US 2006<br>PRIORITY APP | BF, BJ,<br>063<br>278039<br>914<br>AT, BE,<br>IE, SI,<br>0058363<br>LN. INFO | CG,<br>A1<br>A1<br>A1<br>DE,<br>LV,<br>A1 | CI,<br>DK,<br>FI, | CM,<br>2004<br>2004<br>2005<br>ES,<br>RO,<br>2006 | GA,<br>0506<br>0513<br>0817<br>FR,<br>MK,<br>0316 | GN,<br>GB,<br>CY, | GQ,<br>CA 2<br>AU 2<br>EP 2<br>GR,<br>AL,<br>US 2<br>US 2 | GW,<br>003-<br>003-<br>1T,<br>TR,<br>005-<br>002- | ML,<br>2503<br>2780<br>7691<br>LI,<br>BG,<br>5302<br>4202 | MR,<br>063<br>39<br>22<br>LU,<br>CZ,<br>14<br>92P | NE,<br>NL,<br>EE, | SN,<br>2<br>2<br>2<br>SE,<br>HU,<br>2<br>P 2 | TD,<br>0031<br>0031<br>0031<br>MC,<br>SK<br>0050 | TG<br>021<br>021<br>021<br>PT,<br>404 |     |  |  |

GΙ

$$F_{3}C \xrightarrow{N} \stackrel{0}{\underset{k}{\bigvee}} \stackrel{0}{\underset{k}{\bigvee}} Y_{-L-((CH_{2})_{m}XNO_{n})_{F}}$$

AB Novel compds. of formulas I and II [R = H, alkyl; L = bond, alkylidene, cycloalkylidene, aryl, etc.; X = O, S; Y = bond, S, O, (substituted) NH; m = 0-4; n = 1-2; p = 1-4] are prepared, which are nitric oxide-releasing prodrugs useful in the treatment of cyclooxygenase-2 mediated diseases. The invention also encompasses certain pharmaceutical compns. and methods for treatment of cyclooxygenase-2 mediated diseases comprising the use of compds. I or II. The above compds. may be used as a combination therapy with low-dose aspirint to treat chronic cyclooxygenase-2 mediated diseases or conditions while simultaneously reducing the risk of thrombotic cardiovascular events.

IT 685107-04-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrosated or nitrosylated prodrugs for cyclooxygenase-2 inhibitors)

RN 685107-04-4 CAPLUS

CN Acetamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-2-(nitrooxy)- (CA INDEX NAME)

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 2004:2830 CAPLUS Full-text DOCUMENT NUMBER: 140:59410

TITLE:

SOURCE:

Preparation of nitrooxy derivatives of

cyclooxygenase-2 inhibitors Del Soldato, Piero; Santus, Giancarlo

INVENTOR(S): PATENT ASSIGNEE(S):

Nicox S.A., Fr.

PCT Int. Appl., 27 pp.

CODEN: PIXXD2 DOCUMENT TYPE: Patent.

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

|         |                                |             |      |     | KIND DATE   |     |      |                |                 |                                  | LICAT |     |          |      |      |      |     |  |  |
|---------|--------------------------------|-------------|------|-----|-------------|-----|------|----------------|-----------------|----------------------------------|-------|-----|----------|------|------|------|-----|--|--|
|         |                                |             |      |     |             |     | 2003 | 1231           |                 |                                  |       |     |          | 0030 | 620  |      |     |  |  |
|         | TO 2004000781<br>TO 2004000781 |             |      |     |             |     |      |                |                 |                                  | 2005  |     | 20030020 |      |      |      |     |  |  |
|         |                                |             |      |     |             |     |      |                |                 | BB.                              | , BG, | BR. | BY.      | BZ.  | CA.  | CH.  | CN. |  |  |
|         |                                |             |      |     |             |     |      |                |                 |                                  | EE,   |     |          |      |      |      |     |  |  |
|         |                                |             |      |     |             |     |      |                |                 |                                  | KG,   |     |          |      |      |      |     |  |  |
|         |                                |             |      |     |             |     |      |                |                 |                                  | MW.   |     |          |      |      |      |     |  |  |
|         |                                | PG.         | PH,  | PL, | PT,         | RO, | RU.  | SC.            | SD,             | SE                               | , SG, | SK, | SL,      | TJ.  | TM,  | TN,  | TR. |  |  |
|         |                                | TT,         | TZ,  | UA, | UG,         | US, | UZ,  | VC,            | VN,             | YU                               | , ZA, | ZM, | ZW       |      |      |      |     |  |  |
|         | RW:                            | GH,         | GM,  | KE, | LS,         | MW, | MZ,  | SD,            | SL,             | SZ                               | , TZ, | UG, | ZM,      | ZW,  | AM,  | ΑZ,  | BY, |  |  |
|         |                                | KG,         | KZ,  | MD, | RU,         | ΤJ, | TM,  | AT,            | BE,             | BG,                              | , CH, | CY, | CZ,      | DE,  | DK,  | EE,  | ES, |  |  |
|         |                                | FI,         | FR,  | GB, | GR,         | HU, | ΙE,  | IT,            | LU,             | MC,                              | , NL, | PT, | RO,      | SE,  | SI,  | SK,  | TR, |  |  |
|         |                                |             |      |     |             |     |      |                |                 |                                  | , GW, |     |          |      |      |      |     |  |  |
| IT      | 2002                           | A1 20031229 |      |     |             |     |      |                |                 |                                  |       |     |          |      |      |      |     |  |  |
| CA      | 2491                           | 209         |      |     | A1 20031231 |     |      |                | CA 2003-2491209 |                                  |       |     |          |      | 2    | 0030 | 620 |  |  |
|         |                                |             |      |     | A1 20040106 |     |      |                |                 |                                  |       |     |          |      |      |      |     |  |  |
| EP      | 1517                           |             |      |     |             |     |      |                | EP 2003-738069  |                                  |       |     |          |      |      |      |     |  |  |
|         | R:                             |             |      |     |             |     |      |                |                 |                                  | , IT, |     |          |      |      |      | PT, |  |  |
|         |                                |             | SI,  | LT, |             |     |      |                |                 |                                  | , TR, |     |          |      |      |      |     |  |  |
|         | 1662                           |             |      |     |             |     |      |                | CN 2003-814682  |                                  |       |     |          |      |      |      |     |  |  |
|         | 2005                           | 5308        | 36   |     | T           |     |      | JP 2004-514803 |                 |                                  |       |     |          |      |      |      |     |  |  |
|         | 5370                           |             |      |     |             |     |      |                | NZ 2003-537043  |                                  |       |     |          |      |      |      |     |  |  |
|         | 2004                           |             |      |     |             |     | 2005 |                |                 |                                  |       |     |          |      |      |      |     |  |  |
|         |                                |             |      |     |             |     |      |                |                 | MX 2004-PA12851                  |       |     |          |      |      |      |     |  |  |
|         | 2005                           |             |      |     |             |     |      |                |                 |                                  |       |     |          |      |      |      |     |  |  |
|         |                                |             |      |     | A1          |     | 2006 | 0518           |                 | US 2005-516938<br>IT 2002-MI1391 |       |     |          |      |      |      |     |  |  |
| PRIORIT | Y APP                          | LN.         | TNEO | . : |             |     |      |                |                 |                                  |       |     |          |      |      |      |     |  |  |
|         |                                |             |      |     |             |     |      |                | WO:             | 2003-                            | EP65  | 02  |          | w 2  | 0030 | 620  |     |  |  |

OTHER SOURCE(S): MARPAT 140:59410

Disclosed are new compds. able to release COX-2 inhibitors and NO (no data) having formula M-T-YA-NO2 [wherein M-T = the residue of a COX-2 selective inhibitor (T = SO2NH, SO2NR, CO, O, S, NH, N(SO2R); R = C1-10 alkyl; the COX-2 selective inhibitor, M-TH or M-TOH, has to meet test 2 mentioned in the description); YA = -(B)b0-(C)c0-[b0, c0 = 0,1, with the proviso that b0 andc0 cannot be simultaneously 0; B = TB-X2-TB1; TB = CO, X; X = O, S, NH, NR, R (defined above); TB = CO when T = SO2NH, SO2NR-O, S, NH, or N(SO2R), TB = X when T = CO; TB1 = CO or X (defined above); X2 = a divalent radical selected from the following compds. O or O1, etc. (n1, n2 = 0, 1; R2, R3 = H, Me; Y1 = CH2CH2, CH:CH(CH2)n2; n2 = 0, 1)]] for the treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, Alzheimer's disease, or disorders resulting from elevated levels of COX-2. These compds. including 5-niroxypentanoc acid, 4nitrooxybutyric acid, and 4-nitrooxybutyramide, 2-nitroxymethylbenzoic acid ester derivs. mitigate or remove the known side-effects of COX-2 inhibitors. The inflammatory disorders are selected from the group consisting of, but not limited to, arthritis, rheumatoid arthritis, osteoarthritis, allergic rhinitis, sinusitis, chronic obstructive pulmonary diseases, dermatitis, psoriasis, cystic fibrosis, multiple sclerosis, vasculitis and organ

transplant rejection. The cardiovascular diseases are selected from the group consisting of, but not limited to, atherosclerosis, restenosis, coronary artery disease, angina, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, stroke and myocardial infarct. The gastrointestinal disorders are selected from the group consisting of, but not limited to, inflammatory intestinal disorders, Crohn's disease, gastritis, ulcerative colitis, peptic ulcer, hemorrhagic ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison's syndrome, bacterial infections, hypersecretory states associated with systemic mastocytosis or basophilic leukemia and hyperhystaminemia. The disorders resulting from elevated levels of COX-2 are selected from the group consisting of, but not limited to, angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, tendonitis, bursitis, neoplasia, ophthalmic diseases, pulmonary inflammations, central nervous system disorders, allergic rhinitis, atherosclerosis, endothelial disorders, organs and tissues preservation, inhibition and/or prevention of platelets aggregation. Thus, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-y1]-N-[4- (chloro)butyroyloxymethyl]methanesulfonamide. A solution of chloromethyl (4-chloro)butyrate (1 g, 5.40 mmol) in anhydrous THF (5 mL) was slowly added dropwise in a suspension of N-[6-[(2,4-difluorophenyl)thio]-2,3dihydro-1- oxo-1-inden-5-yl]methanesulfonamide sodium salt (2.04 g, 5.40 mmol) in anhydrous THF (25 mL) and stirred at room temperature overnight to give, after workup and silica gel chromatog., N-[6-[(2,4-difluorophenyl)thio]-2,3dihydro-1-oxo-1-inden-5-y1]-N-[4-(chloro)butyroyloxymethyl]methanesulfonam ide (I). A solution of I (1 g, 1.98 mmol) in MeCN (20 mL) was added with AgNO3 (0.67 g. 3.96 mmol), heated at 80° for 15 h in the absence of light, filtered to remove the silver salt, evaporated under vacuum, and purified by chromatog. on a silica gel column to give with n-hexane/ethyl acetate 8/2 as eluent to give 503 mg N-[6-[(2,4-difluorophenyl)thio]-2,3- dihydro-1-oxo-1-inden-5-yl]-N-[4-(nitrooxy)butyroyloxymethyl]methanesulfon amide.

IT 586347-45-7P

RN

CN

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (USes)

(preparation of nitrooxy derivs. of cyclooxygenase-2 inhibitors for treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, or Alzheimer's disease)

586347-45-7 CAPLUS

Butanamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN ACCESSION NUMBER: 2003:652131 CAPLUS Full-text DOCUMENT NUMBER: 139:214237

TITLE:

GI

AR

Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic

TT

and proliferative diseases Scaramuzzino, Giovanni

PATENT ASSIGNEE(S):

INVENTOR(S):

SOURCE:

Eur. Pat. Appl., 313 pp.

Italy

CODEN: EPXXDW DOCUMENT TYPE: Patent.

LANGUAGE: English FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

|                        | PA. | TENT       | NO. |     |     | KIN | D   | DATE |      |     | APP | LICAT | DATE     |     |     |     |      |     |
|------------------------|-----|------------|-----|-----|-----|-----|-----|------|------|-----|-----|-------|----------|-----|-----|-----|------|-----|
|                        |     |            |     | -   |     |     |     |      |      |     |     |       |          |     |     |     |      |     |
|                        | EP  | EP 1336602 |     |     |     |     |     | 2003 | 0820 |     | EΡ  | 2002- | 20020213 |     |     |     |      |     |
|                        |     | R:         | AT, | BE, | CH, | DE, | DK, | ES,  | FR,  | GB, | GR  | , IT, | LI,      | LU, | NL, | SE, | MC,  | PT, |
|                        |     |            | IE, | SI, | LT, | LV, | FI, | RO,  | MK,  | CY, | AL  | , TR  |          |     |     |     |      |     |
| PRIORITY APPLN. INFO.: |     |            |     |     |     |     |     |      |      |     | EP  | 2002- | 4250     | 75  |     | 2   | 0020 | 213 |

New pharmaceutical compds. of general formula F-(X)q (I) [q=1-5, preferably]1; F is chosen among drugs such as  $\delta$ -tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1-M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = saturated or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a saturated or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, saturated or unsatd., linear or branched 1-21 carbon atom alkyl, saturated or unsatd, optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, C1, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1-M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)40NO2, COCH(NH2)CH20NO2, 3-OC6H4CH20NO2, etc.] were prepared For example, a-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl derivative II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the preparation of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

## IT 586347-45-7P 586347-46-8P 586347-62-8P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

- RN 586347-45-7 CAPLUS
- CN Butanamide, N-[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)

- RN 586347-46-8 CAPLUS
- CN Butanoic acid, 4-[[[4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]amino]-2,3-bis(nitrooxy)-4-oxo- (CA INDEX NAME)

- RN 586347-62-8 CAPLUS
- CN Butanamide, N-[[4-[3-(difluoromethyl)-5-(3-fluoro-4-methoxyphenyl)-1H-pyrazol-1-yl]phenyl]sulfonyl]-4-(nitrooxy)- (CA INDEX NAME)

=> file marpat COST IN U.S. DOLLARS

SINCE FILE

TOTAL ENTRY SESSION 196.34

FULL ESTIMATED COST DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

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-2.40

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1 ANSWERS

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